NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Health Technology Appraisal

Cetuximab for the first-line treatment of advanced and/or metastatic non-small cell lung cancer

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of cetuximab, within its licensed indication, for the first-line treatment of locally advanced and/or metastatic non-small cell lung cancer which over-expresses epidermal growth factor receptor (EGFR) tyrosine kinase (TK).

Background

Lung cancer falls into two main histological categories: around 85-90% are non-small cell lung cancers (NSCLC) and the remainder are small cell lung cancers. Approximately 45% of NSCLCs are squamous cell carcinomas, approximately 45% are adenocarcinomas and approximately 10% are large cell carcinomas. Between 5% and 15% of cases of NSCLC are diagnosed on routine chest radiographic examination, but the majority of cases present with symptoms and signs related either to the site of the growth of the primary tumour, or to the effects of thoracic or metastatic spread. About 30% of patients present with locally and regionally advanced disease (Stage IIIb) and 40% with advanced disease (Stage IV) in which the cancer has spread to other parts of the body or there are other symptoms such as a build up of fluid around the lungs or heart (known as pleural or pericardial effusion).

In England and Wales 34,949 people were diagnosed with lung cancer in 2008 with 30,254 deaths registered in 2008. The prognosis for patients with NSCLC is poor, with one-year survival rate of 28% and a five-year survival rate of 8%. Lung cancer incidence and mortality rates are strongly associated with smoking and socio-economic factors.

About 20% of patients with NSCLC have disease which is suitable for potentially curative surgical resection. However, for the majority of NSCLC patients, the aims of therapy are to prolong survival and improve quality of life. Treatment may include radiotherapy and supportive care with or without chemotherapy. NICE has published a clinical guideline on the diagnosis and treatment of lung cancer (CG121). It recommends that chemotherapy should be offered to patients with stage III or IV NSCLC and a good performance status. This should be a combination of one of gemcitabine, docetaxel, paclitaxel, vinorelbine with a platinum drug (carboplatin or cisplatin). Patients who are unable to tolerate a platinum combination may be offered single-agent chemotherapy. NICE technology appraisal 181 recommends pemetrexed in combination with cisplatin as an option for the first-line treatment of locally advanced or metastatic NSCLC if the histology of the

tumour has been confirmed as adenocarcinoma or large-cell carcinoma. NICE also recommends gefitinib as an option for the first-line treatment of people with locally advanced or metastatic NSCLC if they test positive for the EGFR-TK mutation (NICE Technology Appraisal 192).

The technology

Cetuximab (Erbitux, Merck Serono) is an anti-epidermal growth factor receptor (EGFR) monoclonal antibody. Cetuximab prevents the proliferation of cells by binding to the extracellular part of EGFR and preventing autophosphorylation of the intracellular region. This stops cells from dividing. Cetuximab may also make the cancer cells more sensitive to chemotherapy.

Cetuximab has a marketing authorisation for the treatment of patients with EGFR expressing, KRAS wild-type metastatic colorectal cancer and for patients with squamous cell cancer if the head and neck but does not currently hold a UK marketing authorisation for NSCLC. Cetuximab has been studied in clinical trials in people with EGFR expressing (demonstrated by an immunohistochemical test), advanced and/or metastatic NSCLC in combination with cisplatin and vinorelbine versus cisplatin and vinorelbine alone.

Intervention(s)	Cetuximab in combination with other chemotherapy as a first-line treatment
Population(s)	People with locally advanced and/or metastatic non-small-cell lung cancer which over-expresses EGFR
Comparators	Platinum based chemotherapy (carboplatin or cisplatin) in combination with gemcitabine, docetaxel, paclitaxel or vinorelbine EGFR inhibitors: • Gefitinib For people with non-small cell lung cancer other than predominantly squamous cell histology: • Pemetrexed in combination with cisplatin or carboplatin
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rate • duration of response • health-related quality of life

	• adverse effects of treatment
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective. The cost of any additional testing not currently routinely undertaken that is required for this treatment should be considered in the economic analysis.
Other considerations	Guidance will only be issued in accordance with the marketing authorisation. If evidence allows, subgroups of patients defined by, histology (such as tumour cell types) or other relevant factors, will be considered.
Related NICE recommendations	Related Technology Appraisals: Technology Appraisal No. 192, July 2010, 'Gefitinib for the first-line treatment of locally advanced or metastatic non-small-cell lung cancer'. Review date April 2013. Technology Appraisal No. 181, September 2009, 'Pemetrexed for the first-line treatment of non-small-cell lung cancer'. Review date TBC. Technology Appraisal No. 176, August 2009, 'Cetuximab for the first line treatment of metastatic colorectal cancer'. Review date August 2012. Technology Appraisal No. 162, November 2008, 'Erlotinib for the treatment of non-small-cell lung cancer'. Currently being considered for review. Technology Appraisal No.148, June 2008, 'Bevacizumab for the treatment of non-small-cell lung cancer' (terminated appraisal). Technology Appraisal No. 145, June 2008, 'Cetuximab for the treatment of head and neck cancer'. Review date TBC. Technology Appraisal No. 124, August 2007,

	'Pemetrexed for the treatment of non-small-cell lung cancer'. Review date TBC. Technology Appraisal in development, 'Erlotinib monotherapy for the maintenance treatment of non-small-cell lung cancer'. Earliest anticipated publication TBC. Technology Appraisal in development, 'Erlotinib for the first-line treatment of EGFR mutation non-small-cell lung cancer'. Earliest anticipated publication April 2012. Technology Appraisal in development, 'Cetuximab (mono- or combination chemotherapy), bevacizumab (combination with non-oxaliplatin chemotherapy) and panitumumab (monotherapy) for the treatment of metastatic colorectal cancer after first-line chemotherapy (review of technology appraisal 150 and part-review of technology appraisal 118).' Earliest anticipated publication TBC. Related Guidelines: Clinical Guideline No.121. April 2011, 'The diagnosis and treatment of lung cancer' (update of Clinical Guideline 24). Review date TBC.